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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,938	01/09/2007	Catharina Svanborg	BJS-4984-7	2661

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EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,938	SVANBORG, CATHARINA	
	Examiner	Art Unit	
	ANAND U. DESAI	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-35,37 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-35,37 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060828; 20070906*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copies have been filed in the instant application. The priority date is February 26, 2004.

Information Disclosure Statement

2. The information disclosure statements (IDSs) submitted on August 28, 2006 and September 6, 2007 are being considered by the examiner. The signed 1449 forms are attached with the office action.

Specification

3. The disclosure is objected to because of the following informalities:

4. The title brief description of the drawings is missing in the disclosure. The description of the figures refers to color images, but no petition for color drawing, or color drawing are noted in the file history of the instant application.

Appropriate correction is required.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 22, 29, 37, and 38 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,270,822 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are of overlapping scope. The claims of the issued U.S. Patent are drawn to a method of treating papilloma (proliferative disease) by administering to a patient in need thereof a biologically active complex of alpha-lactalbumin. The active complex of alpha-lactalbumin is known in the art as HAMLET once compelxed with a cis C18 unsaturated fatty acid cofactor.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 22-35, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating tumors in a patient comprising administering to a patient in need thereof, a biologically active complex of alpha-lactalbumin in

the apo folding state (partially unfolded state), complexed with either cis C18:1:9 (oleic acid) or cis 18:1:11 (vaccenic acid), does not reasonably provide enablement for any biologically active complex comprising any alpha-lactalbumin with any cofactor to treat any tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) eight factors are addressed in determining enablement.

1.) The nature of the invention: the invention is drawn to a biologically active complex comprising alpha-lactalbumin, selected from HAMLET (human alpha-lactalbumin made lethal to tumor cells) or a biologically active modification thereof, or a biologically active fragment of either of these for the use in the treatment of proliferative disease and/or to inhibit angiogenesis.

2.) The breadth of the claims: the claims are extremely broad in that a very large number of constituents could be encompassed by biologically active modifications, or a biologically active fragment of alpha-lactalbumin.

4.) & 5.) The amount of direction or guidance presented:/The presence or absence of working examples: the example of using HAMLET generated on an C18:1:9 (oleic acid) conditioned ion-exchange chromatography column to isolate a complex which can be used treat tumors on patients do not in any way suggest that modifications, fragments, and variants of the alpha-lactalbumin protein, or any cofactor would have the conformations necessary to be used in treating tumors. The specification provides guidance with respect to the oleic acid discussed in the working example as the cofactor, but provides no guidance whatsoever in selecting which other cofactors might have the needed structure to stabilize HAMLET.

3.) The predictability or unpredictability of the art: / 6.) The quantity of experimentation: there is predictability in the art with regard to the stereo-specific lipid-protein interactions required to form HAMLET. Svensson et al. describe complexes of apo-alpha-lactalbumin with the cofactor of unsaturated C18 fatty acids in the cis configuration that have apoptotic activity on tumor cells. Svensson et al. state that saturated C18 fatty acids, unsaturated fatty acids in the trans configuration, or fatty acids with shorter carbon chains could not form HAMLET (see Discussion, page 2810, 1st sentence on left column of text). There is undue experimentation because of variability in prediction of apoptotic activity in the presence of different cofactors that can form biologically active complexes with HAMLET.

7.) The state of the prior art: the prior art has shown alpha-lactalbumin can alter its biological function depending on the conformational state. The conversion to HAMLET requires the partial unfolding of alpha-lactalbumin. The biological apoptotic activity requires the presence of C18:1 fatty acids (see 11/8/04 IDS document, Svensson et al., PNAS, Discussion, page 4225, paragraphs 1 through 3).

8.) Level of skill in the art: the level of skill in this art is high, at least that of a doctoral scientist with several years of experience in the art.

In consideration of each of factors discussed above, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

9. Claims 22-35, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are directed to a method of treating humans for proliferative disease and/or inhibiting angiogenesis, which comprises administering to a patient a biologically active complex of alpha-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, Paragraph 1, "Written Description" Requirement, published at Federal Register, Vol. 66, No. 4, pp. 1099-1111 outline the method of analysis of claims to determine whether adequate written description is present. The first step is to determine what the claim as a whole covers, i.e., discussion of the full scope of the claim. Second, the application should be fully reviewed to understand how applicant provides support for the claimed invention including each element and/or step, i.e., compare the scope of the claim with the scope of the description. Third, determine whether the applicant was in possession of the claimed invention as a whole at the time of filing. This should include the following considerations: (1) actual reduction to practice, (2) disclosure of drawings or structural chemical formulas, (3) sufficient relevant identifying characteristics such as complete structure, partial structure, physical and/or chemical properties and functional characteristics when coupled with a known or disclosed correlation between function and structure, (4) method of making the claimed invention, (5) level of skill and knowledge in the art and (6) predictability of the art. For each claim drawn to a single

embodiment or species, each of these factors is to be considered with regard to that embodiment or species. For each claim drawn to a genus, each of these factors is to be considered to determine whether there is disclosure of a representative number of species that would lead one skilled in the art to conclude that applicant was in possession of the claimed invention. Where skill and knowledge in the art is high adequate written description would require fewer species to be disclosed than in an art where little is known; further, more species would need to be disclosed to provide adequate written description for a highly variable genus.

First, what do the claims as a whole cover? Claims are directed to a method of treating proliferative disease and/or inhibit angiogenesis using a biologically active complex of alpha-lactalbumin, selected from HAMLET or a biologically active modification thereof, or a biologically active fragment of either of these. The claims are also drawn to a method of treating tumors, comprising administering a biologically active complex of alpha-lactalbumin, which includes any cofactor, which stabilizes the complex in a biologically active form. The claims are drawn to biological active modifications and fragments of human alpha-lactalbumin, HAMLET.

Second, how does the scope of the claims compare to the scope of the disclosure? The disclosure contains the same language found in claims and also discloses the specific complex comprising cis C18:1:9 fatty acid with the partially unfolded state of human alpha-lactalbumin. Thus, the specification is more detailed than claims.

Third, the factors need to be considered.

(1) What was actually reduced to practice?

The species comprising a partially unfolded state of human alpha-lactalbumin, complexed with cis C18:1:9 fatty acid is reduced to practice to treat tumors in patients in need thereof.

(2) Is there disclosure of drawings or structural chemical formulas?

There is no disclosure of how the alteration of alpha-lactalbumin results in a structure that gives rise to HAMLET activity in the presence of cis C18:1:9 fatty acid that is useful to treat tumors.

(3) Are there sufficient relevant identifying characteristics disclosed?

There are insufficient relevant identifying characteristics disclosed for the genus of modified or fragments of alpha-lactalbumin complexes identified as HAMLET. The disclosure does not direct one of ordinary skill in the art to a genus of modified HAMLETs that function as currently claimed. The structural modifications are not disclosed.

(4) Is there at least one method of making the claimed invention disclosed?

One of skill in the art could easily produce the complex of human alpha-lactalbumin with cis C18:1:9 fatty acid as disclosed on page 10, lines 26-35, since only basic chromatography skills would be needed.

(5) What is the level of skill in the art and what knowledge is present in the art?

The level of skill in the art of protein pharmaceutical chemistry is high, about that of a PhD scientist with several years experience.

(6) What is the level of predictability of the art?

There is predictability in the art with regard to the stereo-specific lipid-protein interactions required to form HAMLET. Svensson et al. describe complexes of apo-alpha-lactalbumin with the cofactor of unsaturated C18 fatty acids in the cis configuration that have apoptotic activity on tumor cells. Svensson et al. state that saturated C18 fatty acids, unsaturated fatty acids in the trans configuration, or fatty acids with shorter carbon chains could not form HAMLET (see Discussion, page 2810, 1st sentence on left column of text).

Thus, having analyzed the claims with regard to the Written Description guidelines, it is clear that the specification does not disclose a representative number of species which would lead one skilled in the art to conclude that applicant was in possession of the claimed invention.

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANAND U. DESAI whose telephone number is (571)272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

January 21, 2009
/ANAND U DESAI/
Primary Examiner, Art Unit 1656